REMARKS

In the Office Action dated May 19, 2004, claims 39-47, 52, and 53, all of the claims under consideration of the subject patent application, were rejected. The Examiner has withdrawn new claims 48-51 because these claims are seen by the Examiner to be independent and distinct from the originally elected invention. By amendment above, claims 39, 52, and 53 have been rewritten. Support for the amendments in claims 39, 52 and 53 can be found on page 6 lines 29-31 and on page 4, lines 24 to 27 of the specification.

Reconsideration of this application and allowance of the claims is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 39-47 and 53 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. According to the Examiner, new claims 39-47 and 53 introduce new matter into the claims since the specification as originally filed does not provide support for the negative limitation, "the ibuprofen medicament does not contain a calcium salt of ibuprofen in combination with an alkali metal salt of ibuprofen." The Examiner asserts the calcium salt is one of the preferred salts disclosed as the instant invention as on page 7, lines 14-17 of the specification. According to the Examiner any negative limitation or exclusionary proviso must have basis in the original disclosure.

Applicant submits that the negative limitation is supported by the specification because this limitation was included in the claims as originally filed. Applicant submits that when claims 39-47 and 53 were introduced into this application, applicants specifically referred to these

original claims (claims 1-10, 16-19, 26, 30 and 31) for support of claims 39-47 and 53. Upon request Applicant offers to amend the specification to include the limitations of the cancelled claims as originally filed. Therefore, Applicant submits claims 39-47 and 53 are supported by the specification as under 35 USC §112, first paragraph. Withdrawal of the rejection is respectfully requested.

Claims 39-47, 52 and 53 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Geyer et al. (US 5,380,535) in view of Gregory et al. (US 5,262,179). According to the Examiner, Geyer et al discloses chewable compositions for oral delivery of unpalatable drugs. Further, the Examiner asserts that Geyer et al discloses the compressable fillers of claims 8 and 31 and the disintegrating components of claims 9 and 30. Moreover, according to the Examiner Geyer et al discloses a powder that can be compressed into a tablet comprising ibuprofen, a compressible filler, a disintegrant, sodium bicarbonate, lubricants and flow aids. However the reference does not disclose the crushing strength, disintegration time or compression force as instantly claimed, a salt of ibuprofen or a solid formulation having a layer as instantly claimed. Further, Geyer et al. does not expressly disclose the employment of the particular sodium carbonate or sodium bicarbonate in 3-20% by weight in the ibuprofen dosage, and that the particular sodium salt of ibuprofen may be 40-60%. According to the Examiner Gregory et al discloses masking the unpleasant taste of ibuprofen salts by incorporating an alkali metal bicarbonate into the dosage form. The Examiner asserts that it would have been obvious to employ the particular sodium carbonate or sodium bicarbonate and 3-20% ibuprofen and to optimize the amounts of sodium carbonate or sodium bicarbonate. Further, the Examiner asserts that one of ordinary skill in the art would select optimal parameters to obtain beneficial effects.

Applicant submits that claims 39-47, 52 and 53, as amended are distinct and nonobvious over Geyer et al in view of Gregory et al. In particular, the dosage forms as now claimed are not adapted to be dissolved or dispersed in water prior to administration (see page 6, lines 29 to 31), which is in complete contrast to the disclosure of Gregory et al.

Moreover, the compressed dosage form as claimed is adapted for direct oral administration by swallowing and to disintegrate quickly in the gastro-intestinal tract (i.e. the dosage form is such that it is swallowed whole and is adapted to disintegrate in the gastro-intestinal tract). In contrast to Geyer et al., the claimed compressed dosage form is not of a suitable form (i.e. size, hardness, etc) so it may be chewed and disintegrate in the oral cavity. In this respect, it is clear from Geyer et al. (column 1, lines 23 to 45) that the problems associated with masking the taste of drugs are significantly reduced, if not eliminated all together, for dosage forms which are swallowed whole, particularly solid compressed dosage forms such as tablets, compared with dosage forms where the drug is in contact with the oral cavity for prolonged periods of time. Such dosage forms where the drug is in contact with the oral cavity for prolonged periods of time include masticable dosage forms as disclosed in Geyer et al., as the drug is released in the oral cavity, and aqueous solutions of dosage forms as disclosed in Gregory et al., where a dilute solution of the drug passes over the oral mucosa upon administration to a patient. In summary, an extremely small proportion of the active ingredient within a compressed solid dosage form is exposed to the oral mucosa if the dosage form is swallowed whole, as the active ingredient is enclosed within the dosage form and therefore not exposed to the oral mucosa and the active ingredient is released in the gastro-intestinal tract as opposed to the oral cavity.

Thus, it is typically not necessary to consider taste masking active agents for compressed dosage forms which are swallowed whole.

In light of the above, Applicant respectfully submits that a skilled person would not even consider Geyer et al. or Gregory et al., let alone combine the teaching of these references, in an attempt to provide a compressed solid dosage form adapted to be swallowed whole and having the advantages as discussed hereinafter, as the taste masking issues discussed in Geyer et al. and Gregory et al. are not applicable to dosage forms that are swallowed. In addition, the combination of Geyer et al. and Gregory et al. appears most unlikely due to the reasons put forward in Applicant's response to the previous Office Action.

Therefore, applicant submits that the use of sodium bicarbonate or sodium carbonate in a compressed dosage form of the sodium salt of racemic ibuprofen is not obvious over the combination of Geyer et al. and Gregory et al. Applicant respectfully submits that the claimed invention of claims 39-47, 52, and 53 therefore is not obvious over Geyer et al. (US 5,380,535) in combination with Gregory et al. (US 5,262,179). Withdrawal of the rejection is respectfully requested.

Claims 39-47, 52 and 53 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Armitage et al. (WO 9220334) in view of Gregory et al. (5,262,179). According to the Examiner, Armitage et al. et al disclose "a pharmaceutical composition comprising ibuprofen salt in racemic mixture of S-ibuprofen, such as alkaline earth metal salts, for example the sodium salt of ibuprofen, and a carrier, a compressible filler component such as lactose, microcrystalline, and calcium phosphate, combined with a disintegrating component such as maize starch and lubricating agents." The Examiner asserts that Armitage et al. et al also

discloses the effective amounts of the ingredients. However, according to the Examiner the cited Armitage et al. does not expressly disclose the employment of the particular sodium carbonate or sodium bicarbonate 3-20% by weight in the ibuprofen dosage of Armitage et al. and the particular amount of sodium salt of ibuprofen. According to the Examiner, Gregory et al discloses masking the unpleasant taste of ibuprofen salts by incorporating an alkali metal bicarbonate into the dosage form. Specifically, the Examiner asserts that Gregory et al disclose the particular amounts of the ingredients as claimed in the present invention. According to the Examiner it would have been obvious to employ the particular sodium carbonate or sodium bicarbonate in 3-20% by weight in the ibuprofen dosage of Armitage et al. et al and to optimize the amount of sodium salt of ibuprofen. According to the Examiner, the motivation to combine Gregory et al with Armitage et al. et al is that it was known that ibuprofen salts have an unpleasant taste and it is advantageous to provide a dosage form which will mask this unpleasant taste by incorporating the sodium carbonate or sodium bicarbonate according to Gregory et al. Therefore, the Examiner asserts the claimed invention is obvious over the teachings of the prior art.

In response to the Examiner, Applicant submits that Armitage et al. aims to solve a completely different problem than Gregory et al. and also from the problem addressed by the invention of the present application. Armitage et al. is directed to providing the active enantiomeric form of salts of ibuprofen, namely S(-)sodium ibuprofen, processes for preparing such salts and pharmaceutical compositions containing them. Armitage et al. is not concerned whatsoever with masking the taste of such salts, even if they do indeed exhibit a poor taste. Thus, Armitage et al. and Gregory et al. aim to solve completely different technical problems and a

skilled person would not readily combine the teachings of these documents. Contrary to the Examiner's opinion, Armitage et al. is not concerned whatsoever with the sodium salt of racemic ibuprofen as claimed in the present invention. As discussed above, Gregory et al. is directed to taste masking aqueous solutions of water soluble ibuprofen salts in aqueous solution. For solid dosage forms which are swallowed whole, taste masking considerations (i.e. Gregory) do not come into play. Moreover, Armitage et al. does not teach or suggest that the particular enantiomeric salt of ibuprofen disclosed therein has a poor taste. This appears to be an unfounded assumption by the Examiner, particularly as it is common general knowledge that particular enantiomers may have different physical properties than racemic mixtures. In this respect, Applicant refers to page 2, paragraph 1 and the bridging paragraph of pages 2 to 3 of Armitage et al.

As mentioned above, the invention of the present application provides an improved compressed dosage form which is swallowed whole and permits delivery of high therapeutic levels of the sodium salt of racemic ibuprofen to the gastrointestinal tract of a patient.

As stated in the present application at page 7, the sodium salt of racemic ibuprofen is a flaky, soft and sticky material. Consequently, it does not lend itself to formulation into a directly compressed dosage form as it typically sticks to the tabletting punches. Moreover, it is also difficult to pre-granulate the sodium salt prior to compression with other excipients. In order to form satisfactory compressed dosage forms of the sodium salt of racemic ibuprofen it is necessary to pre-treat the salt, i.e. milling, etc.

Unexpectedly, the inclusion of sodium bicarbonate or sodium carbonate in the carrier material permits the formation of a satisfactory compressed dosage form of the sodium salt of

racemic ibuprofen without the need to initially pre-treat the ibuprofen. Conveniently, it is therefore possible to use sodium ibuprofen taken directly from a bulk production process, thereby significantly reducing the overall production costs (see page 7, lines 28 to 31 and page 2, lines 12 to 14).

In addition, the inclusion of sodium bicarbonate or carbonate also enhances the compressibility of the pharmaceutical composition comprising the compressible filler and disintegrant. Particularly, the composition used to form the compressed dosage form may be compressed by applying compression forces of standard tabletting machines to produce a compressed dosage form which exhibits improved hardness (i.e. so that it does not break up during further manufacturing steps) while maintaining an acceptable relatively fast disintegration time to permit an on-set hastened action (see page 2, lines 1 to 20, page 3, lines 8 to 14). This effect is clearly demonstrated by the results of Tables 1 and 2 and commentary thereon at page 31. The inclusion of sodium bicarbonate or carbonate permits a reduction in the overall amount of compressible filler thereby allowing production of an acceptably sized tablet including a large therapeutic dose of the sodium salt of racemic ibuprofen (page 2, lines 4 to 8 and page 3, lines 7 to 10).

In contrast, Armitage et al. explicitly states that the particular enantiomeric sodium salt of ibuprofen disclosed therein exhibits improved tabletting properties and does not stick to the punches of the tablets (see page 2, paragraph 1, bridging paragraph of pages 2 to 3, page 23, lines 16 to 17). This is in complete contrast to the sodium salt of racemic ibuprofen as used in the invention of the present application. Thus Armitage et al. provides a completely different solution to the same problem solved by the present invention and therefore teaches away from

the present invention. As mentioned above, Gregory et al. also solves a completely different technical problem than the one solved by the invention of the present application.

Applicant respectfully submits that the claimed invention in claims 39-47, 52, and 53 therefore is not obvious over Armitage et al. (WO 9220334) in combination with Gregory et al. (5,262,179). Withdrawal of the rejection is respectfully requested.

Applicant submits that the present application is now in condition for allowance. Reconsideration and favorable action are earnestly requested.

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